SACHET FOR A PHARMACEUTICAL COMPOSITION

Field of the Invention

The present invention concerns a sachet for a pharmaceutical composition.

The present writ claims priority from the Danish patent application PA 2003 00612, The European patent application EP 03388023, and the US provisional patent application 60/464649.

Technical Background

Oral pharmaceutical formulations comprising mesalazine are known, which are either tablets or granulate. Granulate may be packed in sachets. For the purposes of the present invention a "sachet" will refer to an envelope or bag for a granulate, while "granulate" refers to particles, granulate or spheronised particles.

Known sachets tend to suffer from the draw back of complicated manufacturing methods or high production costs. In order to being accepted by consumers, a sachet should preferably be easy to open without the use of scissors. Upon pouring granulate from a sachet preferably as little material as possible should be lost. Static electricity may build up between certain granulate types and sachets. This is dependent of the type of granulate as well as the type of sachet. If static electricity is present, it tends to be difficult to pour granulate from the sachet. Finally, granulate in a sachet may be sensitive to degradation by light, humidity and/or air. This is also dependent of the type of sachet as well as the type of granulate.

Disclosure of the Invention

These problems and others mentioned below are addressed by aspects of the invention.

For the purposes of the present invention the term "mesalazine" also encompasses pharmaceutically acceptable salts and esters thereof, such as those mentioned in WO 97/23199 p. 15, l. 17 - p. 6, l. 12, as well as prodrugs, such as balsalazide.

The formulation, to be stored in a sachet according to the invention, is preferably in the form of a particulate material, e.g. granulate, spheres, pellets, particles, preferably granulate.

The present sachet may be used for any pharmaceutical formulation, but is especially suitable for storing pharmaceuticals comprising sensitive compounds such as mesalazine.

According to an aspect, the present invention concerns a sachet, comprising the layers:

i) paper;
ii) bonding layer, preferably an adhesive such as polyethylene;
iii) barrier layer, preferably aluminium foil; and
iv) sealing layer, preferably low density polyethylene.

Mesalazine is sensitive to humidity, atmospheric air and/or light. A sachet for a product containing mesalazine should therefore preferably provide a barrier to humidity, atmospheric air and light. The sachet should also be easy to open for a patient, preferably without the use of additional tools, such as scissors. It has been a problem to provide a sachet with the necessary barrier properties without sacrificing the possibility of tearing open the sachet with human fingers. Further, existing sachets tend to suffer from the build up of static electricity. Preferably, a sachet should be easy

to manufacture, easy to fill, easy to empty, and have an appealing look to improve patient compliance.

This aspect provides a sachet giving long storage stability for a pharmaceutical composition contained therein, e.g. where the active pharmaceutical ingredient is mesalazine. Further, the sachet is easy to tear and static electricity is eliminated, providing for a sachet which may be emptied completely for its contents. The combination of the sachet and the oral formulation according to the present invention provides for little build up of static electricity.

The outer paper i) has in a preferred embodiment a weight per unit area of 10-100 g/m^2, preferably 30-70 g/m^2, more preferred 40-60 g/m^2, most preferred 50 g/m^2.

Paper having a weight per unit area outside the range of 10-100 g/m^2 are hardly suitable in industrial manufacturing of sachets. Paper having a weight per unit area below about 30-40 g/cm^2 tend to break in manufacturing equipement for sachets. For paper having a weight per unit area above about 60-70 g/cm^2 it is difficult to shape the material to sachets. Optimal results have been achieved with a weight per unit area above of about 50 g/cm^2.

According to an aspect, the bonding layer ii) preferably has a weight per unit area of 6-20 g/m^2, preferably 9-18 g/m^2, more preferred 12-15 g/m^2. If a very thin layer is used, it usually neccesitate the use of expensive special polymers to achieve an appropriate coverage. If a thick layer is applied, it inherently more expensive and hard to avoid an uneven layer.

According to an aspect, the barrier layer iii) preferably has a thickness of 6-30 µm, more preferred 7-25 µm,

preferably 9-25 μm, more preferred 8-20 μm, preferably 9-15 μm, more preferred 12 μm.

Sachet according to any of the preceding claims, wherein said sealing layer iv) has a thickness of 15-50 μm. If a very thin layer is applied, it has a tendency not to cover the surface completely. If a very thick layer is applied, it is hard to weld through, and any heating applied may not warm evenly.

According to an aspect, the sealing layer iv) preferably has a weight per unit area of 10-100 g/m^2, more preferred 15-75 g/m^2, preferably 20-50 g/m^2, more preferably 30-40 g/m^2, most preferred 35 g/m^2.

According to an aspect, the present invention concerns the use of the sachet for a pharmaceutical composition according to the invention.

The sachet has proven suitable for storing the pharmaceutical compositions according to the invention.

According to an aspect, the present invention concerns the use of the sachet for medical purposes.

A sachet according to the present sachet is especially suitable for a pharmaceutical formulation comprising mesalazine or a pharmaceutically acceptable salt thereof.

The present sachet has a remarkably low tendency to build up static electricity. This has formerly especially been a problem with mesalazine granulate. As an example of such a mesalazine product may be mentioned granulate obtainable according to the patent application PCT/DK01/00677.

According to an aspect of the present invention it is not limited to the use of mesalazine as the active ingredient in granulate in the present sachet, but also relates to other active ingredients, such as the ingredients mentioned in WO 00/44353, p. 12-16.

According to an aspect of the present invention further excipients may be comprised in the composition according to the invention, such as fillers, disintegrants, pH adjusters, or surfactants. Such excipients are well known from the literature, see e.g. WO 00/44353, p. 16-20, for a number of suitable excipients.

Some excipients are hygroscopic. As an example of such excipient povidone may be mentioned. If an active ingredient is to be formulated with a hygroscopic excipient, the need for a suitable sachet is emphasized. The present sachet is suitable for being used for pharmaceuticals comprising at least one hygroscopic excipient.

Example

The material of a sachet had the following composition:

Paper, claycoated	50 g/m^2
Polyethylene, low density	12 g/m^2
Aluminium foil	12 µm
Polyethylene, low density	35 g/m^2

For the present example 12 g/m^2 PE corresponds to 13 µm, and 35 g/m^2 PE corresponds to 38 µm. The material had a grammage of 129 g/m^2. The permeability to water vapour was <0.05 g/m^2, 24 h, 25°C, 75% RH, and to O_2 <0.05 ml/m^2, 24 h, atm, 23°C, 75% RH.

The sachets were folded around the filling tube of a filling/sealing station, such that the paper was on the outside of the sachet, and then sealed lengthwise, with a low density polyethylene as a sealing layer. After

forming the cross seal at the bottom the sachet is filled with granulates, and then sealed again at the top and finally cut.

All citations are incorporated in their entirety by reference.